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TROPICAL MEDICINE REVISITED

After an absence of 25 years, The Rockefeller Foundation is launching a major, worldwide, cooperative effort. Why?

by Kenneth S. Warren, M.D.
and Henry Romney

The facts speak for themselves. Each year 150 million people become gravely ill with malaria; this is only an estimate, but that about one million children *die* each year of malaria in Africa alone is a hard fact.

Schistosomiasis is a fluke-worm-caused disease, widely prevalent in Africa, Asia, South America, and the Caribbean, which affects between 200 and 300 million people; children are particularly vulnerable. In one form of the disease, their urine is red with blood and in another they may suddenly regurgitate a pint of blood.

Filariasis, of whose several manifestations river blindness and elephantiasis are the most terrible, affects hundreds of millions of people in Africa, India, and South America. Trypanosomiasis, or African sleeping sickness, described in detail in the last issue of RF Illustrated, is introduced by the bite of the notorious tsetse fly. It is the scourge of Africa.

Leishmaniasis, transmitted by sand flies prevalent in the tropics and the Middle East, in one of its forms gradually erodes the nose, the eyelids, the ears, and even the whole face, producing horrible deformities which do not kill, but make life a travesty. Another form invades the inner organs and is slowly fatal. One billion people harbor *Ascaris*, the foot-long round worm; children may have a hundred or more, and die of intestinal obstruction due to the sheer mass of worms. Then, there is leprosy. . . .

HOW COME?

The phrase "parasitic diseases" is often used interchangeably with tropical diseases. But many of these diseases are truly global problems. Eskimos suffer from trichinosis, pinworms, and the thirty-foot-long fish tapeworm. One protozoan infection (toxoplasmosis), a significant cause of eye disease and birth defects, has infected literally one out of three people in the world. As John H. Knowles points out:

The prevalence of worms in the American people is, in fact, staggering. Nearly 55 million Americans are infested with helminths, the most common of which are pinworms (enterobiasis), giant roundworms (ascaria-

sis), *Trichinella* (trichinosis), and whipworms (trichuriasis). Hookworm infection remains an important public health problem and schistosomiasis has become significant due to Puerto Rican immigrants. Mexican immigrants numbering in the millions have added a whole new host of health problems.

But as threats to life and wellbeing, tropical infectious diseases are of major significance in the poorer countries of the world. There, billions of people are victimized. Their suffering is immense, the social damage in wasted lives, anemic levels of energy, and (because parasitic diseases ravage livestock as well as people) low levels of agricultural productivity is incalculable.

With the state of medicine so far advanced, how could we allow this to happen?

WHO ARE WE?

The answer lies in the history of modern medicine—the evolution of its basic sciences and their social application. It is a relatively short evolution which has culminated in making medicine the speciality par excellence of Western, urbanized man. Understandably, we use that speciality to serve our own perceived needs.

Medical science and technology today is geared overwhelmingly to "conquering" such largely degenerative diseases of rich, urban, old men and women as cancer and the heart diseases. Medical practice centers on the fee-for-service encounter between such patients and their private physicians in a high-technology, hospital setting.

Tropical medicine occupies only a small niche in these research and practice systems because people who suffer from tropical diseases are mostly rural, poor, and, until recently, seldom heard from. The World Health Organization offers a rough estimate that 97 percent of the world funding for biomedical research is spent on health problems that concern the relatively rich countries, and only 3 percent is spent on the diseases that are the scourge of the tropical poor.

"To put it another way," says J. H. Humphrey, professor of immunology at London's Royal Postgraduate Medical School, "the world's total annual research budget for all tropical diseases is about \$30 million a year; one country, the United States, although not ungenerous in its support of tropical

	Prevalence NO. OF PEOPLE (millions)	Funding NO. OF DOLLARS (millions)
CANCER	10	815*
SCHISTOSOMIASIS	200	3
MALARIA	300	5
FILARIASIS	300	<1
AMEBIASIS	400	<1
ASCARIASIS	1,000	<1

*U.S. Government only

Well over two billion people, mostly rural and poor, suffer from parasitic diseases, but over the last several years only between \$10 and \$20 million was spent annually on research. Cancer, much on the mind of the smaller, richer world, draws \$800 million from the U.S. alone.

disease research, spends nine times this amount on cancer research alone.”

THE YEARS OF NEGLECT

Tropical medicine began at the forefront of medical research, coinciding with the palmy days of colonialism, when white administrators and traders were exposed to the hazards of the tropics. For instance, we are told that “85 percent of Europeans going to West Africa in the 19th century died of fever or returned home with their health permanently wrecked.” Any man who announced his departure for West Africa had his life insurance cancelled. Brilliant bursts of investigative accomplishments by such men as Manson in China (elephantiasis), Ross in India (malaria), and Bruce in Africa (sleeping sickness) led to the establishment of institutes of tropical medicine in Europe; in the U.S., the development of schools of public health provided a major locus for research and training in that field, and their accomplishments were many.

But sad to say, their presence may have been an important factor in isolating tropical medicine from the mainstream of biomedical and clinical

research. The medical schools of the developed world felt excused from assuming responsibility for teaching and research in tropical medicine. Since the tremendous growth of multidisciplinary biomedical research in the middle of this century occurred largely in the medical schools, the separate status of tropical medicine has diminished its opportunity to share in the great advances in modern laboratory and clinical investigation.

Decades of neglect have acted to reduce the quantity and quality of biomedical scientists working on tropical diseases and thus have left us bereft of adequate means of combating them. By contrast, this same period has seen a burgeoning of molecular biology, immunology, and biochemistry leading to the production of vaccines (measles, influenza, meningitis, pneumonia, diphtheria) and chemotherapeutic agents (penicillin, streptomycin, tetracycline) for the control of infectious diseases prevalent in the industrial world.

THE TRANSFER OF IGNORANCE

It might be reasonable to expect that in at least the countries most affected, those of the poorer world, available funds and skills would be concen-

COMPARISON OF THE DISCIPLINES OF MICROBIOLOGY AND PARASITOLOGY		
DISCIPLINE:	MICROBIOLOGY:	PARASITOLOGY:
COMPONENT FIELDS:	BACTERIA VIRUSES FUNGI	PROTOZOA HELMINTHS ARTHROPODS
CONSTITUENCY:	DEVELOPED COUNTRIES	DEVELOPING COUNTRIES
CLINICAL COUNTERPART	INFECTIOUS DISEASES	TROPICAL MEDICINE
ACADEMIC LOCALIZATION: (SCHOOLS OF —)	MEDICINE	PUBLIC HEALTH VETERINARY MEDICINE TROPICAL MEDICINE
MAJOR ADVANCES	MOLECULAR BIOLOGY IMMUNOLOGY ANTIBIOTICS VACCINE	INSECTICIDES MOLLUSCICIDES

Great recent advances in medicine have come from microbiological investigations conducted in the main at medical schools, for the benefit of the better-off countries. Tropical medicine, centering on research, usually outside medical schools and with very limited funds, on parasitic diseases, has been the beneficiary of fewer discoveries. In the academic world as elsewhere, it is a truism that talent goes where the money is.

trated on solutions to their own most rampant health problems—infectious parasitic diseases, their ravages greatly exacerbated by malnutrition. But with the export of goods and skills, we also have exported our own values. The result is that even in the poorer countries, medicine, where it exists at all, follows the Western model. In one major medical school in the heart of Africa, structured on the universities of London, tropical medicine was not in the curriculum until the 60's. Large hospitals are built in the cities, absorbing 80 percent of the nation's health budget. They refuse to admit patients with ordinary tropical diseases.

On the level of research—in the heart of Manila stands the Philippine Heart Center. On its inauguration, it was described as the only such institute in the Far East and the third biggest in the world, incorporating the best features of the leading hospitals in the U.S. and Europe.

This magnificent edifice, with its advanced capability for delivering electrocardiograms, phonocardiograms, vectorcardiograms, echocardiograms, rapid X-ray cassette changer facilities, videotape recorders, heart-lung machines, and so forth was built for a country of 40 million people with only 16,000 cardiac deaths a year.

In contrast, the Philippines Schistosomiasis Center on the island of Leyte, a major focus for the study of schistosomiasis japonica, a disease which afflicts 690,000 Filipinos, is a wooden shack.

So much for the health priorities of the Third World, priorities which we have established for ourselves and have exported to a clientele of Third-World politicians and businessmen, themselves members of urban elites and thus appreciative of centers for heart disease and cancer.

NOW THE GOOD NEWS

Today, for the first time in decades, there are definite signs that the tide is turning, signs so unmistakable that those who have had a lifelong interest in tropical medicine are encouraged to think big and act decisively. Here are some of those signs:

- **Scientific Opportunities.** Hitherto "exciting" fields of biochemical investigation (cancer research is only one example) have become so overcrowded and subdivided that gifted investigators in fields such as molecular biology and basic immunology now see new opportunities in the application of their highly relevant talents to the terra incognita of tropical medicine.

Tropical Medicine: Is There a Moral Imperative?

Consider the following case history. An African country, the year, 1974. It had a per capita income of \$62, an infant mortality rate of 20 percent and a life expectancy of thirty years. Every man, woman, and child in the population had malaria, 40 percent had tuberculosis (one out of four with active cases, spitting blood), 25 percent suffered from river blindness (onchocerciasis), 3 percent had leprosy, and 50 percent of children under five died. The national health budget came to less than one dollar per capita. The average health budget for all countries in Africa reporting was U.S. \$1.17 per capita. This is the quality of health and life, differing only in detail, endured by 500 million people in developing nations.

Compare this case with that of the United States, which allocates more than \$500 per capita on health. Ironically, perhaps 60 percent of health care funds are spent on people who will be dead within one year.

Barry R. Bloom
(see "Additional Reading")

- **Altruism.** There is a new spirit of humanitarianism abroad, one summed up well by Howard A. Minners, a high official of the National Institutes of Health, seconded to WHO: "International health comprises a natural and comfortable combination of science and technology with humanitarian concern," Dr. Minners wrote in a recent editorial in *Science* magazine. "The diseased and deprived whole human—not just the parasitic granuloma in his liver or the lepromas in his skin—is becoming of concern."

- **Enlightened Self Interest.** As Dr. Knowles has pointed out on many occasions to audiences as diverse as those of physicians and the directing bodies of multinational corporations: "A shrinking, interdependent, and wormy world cannot afford the stresses of ill health, poverty, disease, and explosive population growth. Solutions abroad can also be applied fruitfully at home and vice versa." Senator Edward Kennedy recently underscored this when, as Chairman of the Subcommittee on Health, he pointed out that "the U.S. contribution to the worldwide smallpox vaccination campaign cost us a total of some \$25 million, but because eradication of this disease enabled us to terminate our own domestic smallpox vaccination program, we are now able to save over \$125 million a year domestically."

- **New Funding.** Ten years ago, the Pearson Report to the World Bank (*Partners in Development*) neglected the relation of health to economic development. Right now, WHO, the World Health Organization, is mobilizing itself for a "Special Program for Research and Training in Tropical Diseases"—a new initiative concentrating, as a beginning, on Africa. The basic avowed purpose is to improve the capability of the developing world to do relevant biomedical research. Incidentally, the estimated cost of the entire research effort on tropical diseases proposed by the WHO is on the order of \$15 million annually—less than three-quarters of the cost of a single F-14 fighter plane.

RETURN OF THE RF

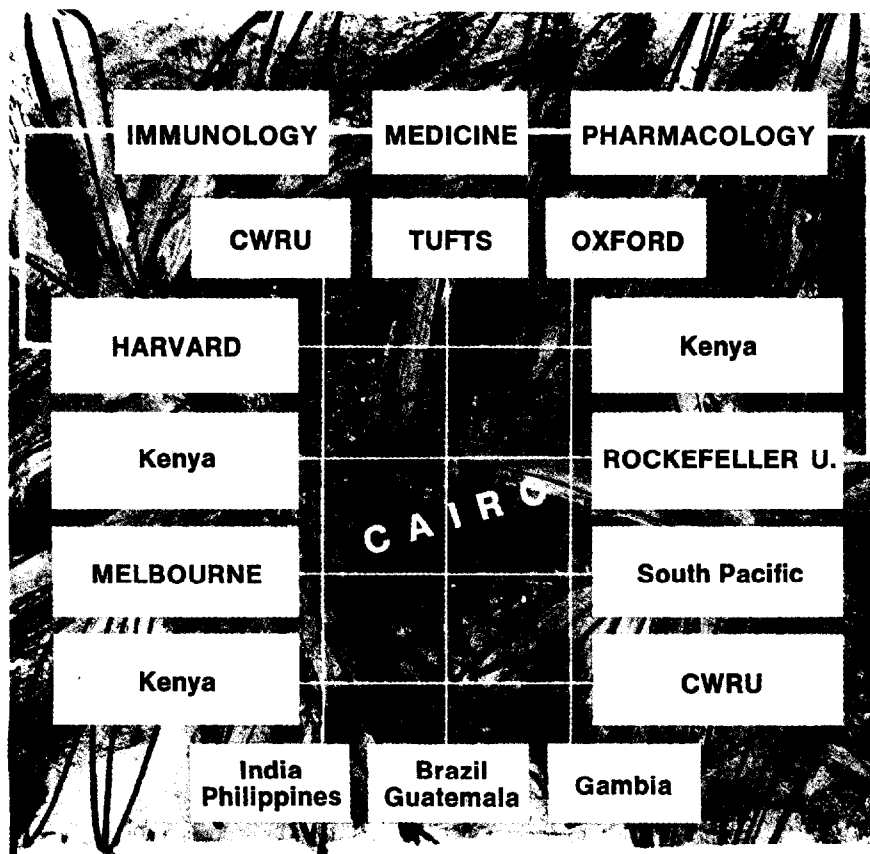
Today, the times appear propitious for The Rockefeller Foundation to return, in a significant and sustained effort, to a field in which, historically, it has played an unmatched role.

The Foundation's International Health Division worked on hookworm, malaria, and yellow fever from 1917 to 1951; the schools of public health and tropical medicine were founded; the base laboratory at The Rockefeller Institute developed a vaccine for yellow fever for which Max Theiler was awarded the Nobel Prize; the Division of Medical Education aided the establishment of the new Flexnerian medical schools in the United States, Europe, and then throughout the world; neuropsychiatry was established as a scientific discipline in medical schools; and modern biological science was revolutionized by the development of molecular biology.

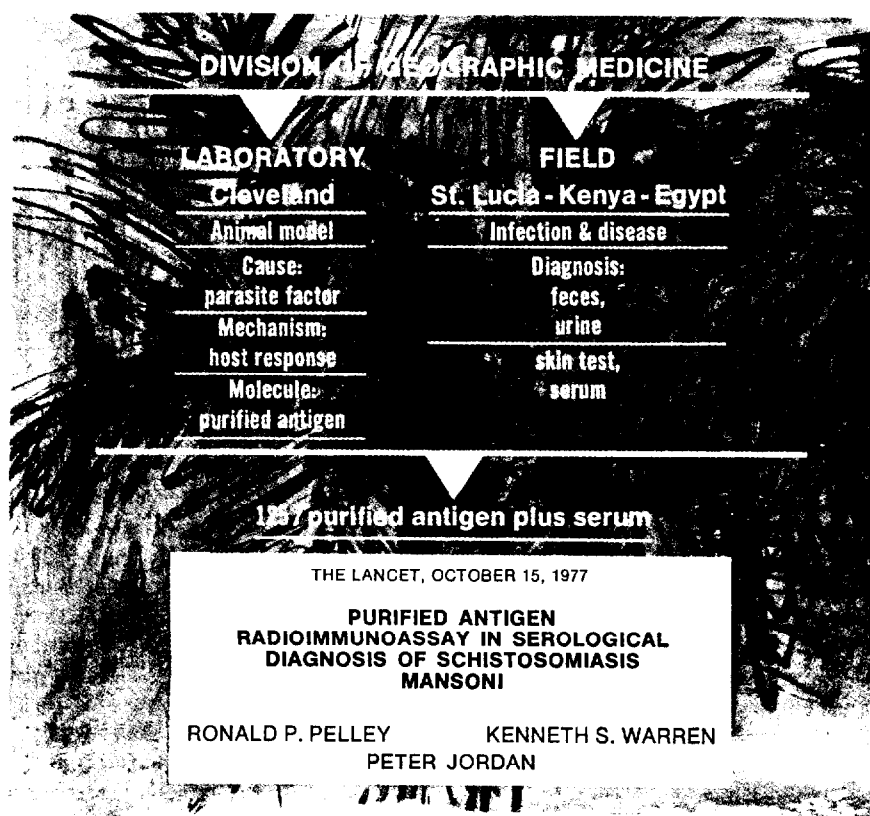
By the early 50's, however, the Foundation's major interest in public health and medicine began to decline. In the 1960's health was included only as an "Allied Interest," until the new program in Population and Health was established in 1973. In 1976, health-related programs were awarded little more than 5 percent of the Foundation's annual expenditure. These included the St. Lucia schistosomiasis program, miscellaneous studies in tropical medicine, and, in the Education for Development program, community health-oriented endeavors.

THE GREAT NEGLECTED DISEASES PROGRAM

Given a new awareness by policymakers of the disastrous implications of tropical diseases on the welfare of hundreds of millions of people, given the enthusiasm of outstanding scientific investigators



A network of outstanding research laboratories here and abroad has been formed to engage the great neglected diseases. Working in one or more fields (immunology, medicine, pharmacology), each research center is linked to field work. (The Cairo facilities are available to each.)



The mutually reinforcing benefits of laboratory and field work are demonstrated by Case Western Reserve's Division of Geographic Medicine. Highly sophisticated immunological research in Cleveland coupled with field work in the Caribbean, Africa, and the Mideast led to the development of a highly specific, rapid, and simple blood test for the diagnosis of schistosomiasis, an achievement reported in a recent issue of *The Lancet*.

for new and challenging fields, given the likelihood that the expenditure of relatively modest funds could have the most beneficial consequences—it is small wonder that enthusiasm exists among the trustees and officers of the RF to play a part in overcoming what we have come to call the Great Neglected Diseases of Mankind.

What the Foundation has set out to do is to create a network of clinical and basic investigative

units led by notable biomedical researchers, each following his own special bent, the sum total of their efforts focused on bringing to the "great neglected diseases" that dimension of scientific excellence so much needed today. The response to our initiative makes us think we are on the right track; at present, the eight units that make up the network are:

- Division of Geographic Medicine, Department of

Medicine, Case Western Reserve University: Dr. Adel A. F. Mahmoud, director. Research Areas—immunity and immunopathology of schistosomiasis, trichinosis, filariasis, giardiasis; pathogenesis and therapy of gram negative bacterial infections; hemoglobinopathies; medical anthropology. Overseas collaborations—Kenya, Egypt, Sudan, India, Guatemala.

- Division of Geographic Medicine, Department of Medicine, Tufts University: Dr. Gerald Keusch, director. Research Areas—bacterial diarrheas, amebiasis, malnutrition. Overseas collaborations—Brazil, Guatemala.

- Tropical Medicine Unit, Department of Medicine, Oxford University, U.K.: Dr. D. Weatherall, director. Research Areas—hemoglobinopathies, malaria. Overseas collaborations—Malaysia, Gambia.

- Pharmacoparasitology Research Unit, Section on Medical Biochemistry, Rockefeller University: Dr. Anthony Cerami, director. Research Areas—biochemistry and treatment of trypanosomiasis and leishmaniasis. Overseas collaboration—Kenya.

- Pharmacoparasitology Research Unit, Department of Pharmacology, Case Western Reserve University: Dr. L. T. Webster, Jr., director. Research Areas—active drug metabolites for treatment of schistosomiasis, filariasis, American trypanosomiasis. Overseas collaboration—Kenya.

- Immunoparasitology Research Unit, Department of Medicine, Robert B. Brigham Hospital, Harvard University: Dr. John David, director. Research Areas—immunity in schistosomiasis, filariasis. Overseas collaborations—Kenya, Egypt, Indonesia.

- Immunoparasitology Research Unit, the Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia: Dr. Graham Mitchell, director. Research Areas—immunity in a variety of helminth and protozoan parasites. Overseas collaborations—Western Pacific.

Biomedical Research Center for Infectious Diseases, Cairo, Egypt: Dr. Aziz El Kholy, director. Research Areas—schistosomiasis, hepatitis, meningitis. Overseas collaborations—available to all members of the network.

ALL TOGETHER NOW

Other units are under consideration in the developed and the less developed worlds. What characterizes the network is this: the institutions and the investigators are first-rate. All will keep in close touch with each other, which includes attending a formal annual meeting (the first is scheduled in New York for November). And most importantly, each unit balances laboratory work with field work in a mutually reinforcing system that can pay great dividends.

The RF-supported network will work closely with WHO's Special Programme for Research and Training in Tropical Diseases, this collaboration being the result of a Memorandum of Understanding now under joint consideration by Dr. Halfdan Mahler, director-general of the World Health Organization, and Dr. John H. Knowles, president of The Rockefeller Foundation.

WHO's orientation is toward strengthening the research capability of the developing world; the RF's is toward establishing a network among the finest biomedical researchers and laboratories wherever in the world they may be found. One can be quite confident that a considerable degree of synergism will result from the close linkages between the two networks.



Dr. Kenneth S. Warren, formerly Professor of Medicine and Geographic Medicine at Case Western Reserve School of Medicine, is an internationally recognized authority on tropical medicine and Director of the RF's Division of Health Sciences.

We are glad to be back. The basic philosophy of our venture cannot be summed up better than it was in 1923 by George Vincent, president of The Rockefeller Foundation:

All that the Foundation is attempting to do, with its relatively limited resources, is to help establish a common front against disease, drawing on the resources and talents of all countries. Whether it is malaria or cholera or plague or tuberculosis or whatever the disease may be, the nations of the world face these enemies of mankind, not as isolated groups behind boundary lines, but as members of the human race projected suddenly into frightening propinquity.

Additional Reading:

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